UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

KD

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/445,517	12/06/99	DUFT	235/013 US

022249
LYON & LYON LLP
SUITE 4700
633 WEST FIFTH STREET
LOS ANGELES CA 90071-2066

HM22/0804

EXAMINER	
DEVI,S	

ART UNIT	PAPER NUMBER
1645	24

DATE MAILED: 08/04/00

Amendment due: 11/4/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

SEP -7 2004

AUG 17 2000

Office Action Summary	Application No. 09/445,517	Applicant(s) Duft et al.
	Examiner S. Devi, Ph.D.	Group Art Unit 1645

☒ Responsive to communication(s) filed on *03/24/2000.*

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-15* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-15* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Change of Art Unit Location

1) Effective 20 June 2000, the Art Unit location of your application in the US PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Technology Center 1600, Group 1640, Art Unit 1645.

Priority

2) The instant application is a 371 of PCT/US98/11753 filed 06/05/98 and a Continuation-in-part of application, SN 08/870,762, filed 06/06/97, now co-pending.

Status of Claims

3) Claims 1-15 are pending in the instant application and are under examination. A First Action on the Merits is issued for these claims.

Abstract

4) This application currently does not contain an abstract of the disclosure as required by 37 C.F.R 1.72(b). However, as this application is filed under 371 with a priority claim to PCT/US98/11753, a copy of the published abstract from PCT/US98/11753 is placed in the instant application as page number 50. If Applicants desired changes to the abstract, such changes should be directed to the abstract of the PCT/US98/11753.

Specification - Informalities

5) The instant specification is objected to for the following reason(s):

(a) The instant specification does not accurately reflect the current co-pending status of the earlier filed application, SN 08/870,762, filed 06/06/97, in the first paragraph of the specification. Amendment to the specification is suggested to provide the current co-pending status of the parent application as indicated in paragraph 2 above.

(b) The spacing of lines in Tables II through VII of the instant specification is such as to make reading and entry of amendments difficult. New pages containing these Tables with double spaced lines on good quality paper are required.

Rejection(s) under 35 U.S.C § 112, First Paragraph

6) Claims 1-10 are rejected under 35 U.S.C § 112, first paragraph, because the specification while being enabling for a method of treating or reducing obesity in a human subject comprising administering an effective amount of an amylin or an amylin agonist, does not reasonably provide enablement for a method of "preventing" obesity in a human subject. Applicants have provided support in the instant specification and examples for a method of "treating" obesity in a human subject comprising administering an effective amount of an amylin or an amylin agonist (see examples). However, no evidentiary support is of record enabling a method of "preventing" obesity in a human subject, diabetic or non-diabetic, by administering an effective amount of an amylin or an amylin agonist, thus requiring undue experimentation to practice the invention as claimed. The specification does not enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims.

Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability of the art; and
- The breadth of the claims.

Based on the instant disclosure, the technology and state of the art at the time of the Applicants' invention, one of ordinary skill in the art would not have been able to produce a method of "preventing" obesity by administration of amylin or amylin agonist. The Webster's II New Riverside University Dictionary defines the term "prevent" as "to keep from happening". The instant specification does not enable such a method wherein administration of amylin or amylin agonist "keeps obesity from happening". The full scope of the claims is not commensurate in scope with the enabling disclosure and the ability to reproducibly practice the full scope of the claimed invention is well outside the realm of routine experimentation, requiring undue experimentation by one of ordinary skill in the art. The enablement (scope) provisions of 35

U.S.C. § 112, first paragraph, are not met and the claims are viewed as non-enabled with respect to their scope.

To be commensurate with the scope of the enabling disclosure, it is suggested that Applicants limit the scope of claims 1-10 to a method of treating obesity in a human subject comprising administering an effective amount of an amylin or an amylin agonist, or provide convincing evidence correlating the claimed method with a broader scope.

Rejection(s) under 35 U.S.C § 102

7) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) The invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

8) Claims 1 and 2 are rejected under 35 U.S.C § 102(b) as being anticipated by Cooper *et al.* (US 5,280,014) ('014), or Cooper *et al.* (US 5,364,841) ('841).

Cooper *et al.* ('014) teach a method of treating obesity in a subject comprising administering an effective amount of CGRP 8-37, which is an amylin agonist (see claims 1 and 11, and column 11, lines 3 and 4).

Cooper *et al.* ('841) teach a method of treating obesity in a subject comprising administering an effective amount of CGRP 8-37, which is an amylin agonist (see claims 2 in combination with lines 7 and 8 of column 11).

Claims 1 and 2 are anticipated by Cooper *et al.* ('014) or Cooper *et al.* ('841).

9) Claims 1-3 are rejected under 35 U.S.C § 102 (e) as being anticipated by Rink *et al.* (US 5,739,106) [Rink *et al.* ('106)].

Rink *et al.* ('106) teach methods for controlling body weight (i.e., treating obesity), reducing food intake and suppressing appetite in mammals including humans using an amylin agonist (see abstract and column 11, lines 25 and 26). Rink's claim 85 is drawn to a method for control of body weight in a mammal (inclusive of humans) comprising administering a

therapeutically effective amount of an amylin agonist such as ^{25,28,29}pro-h-amylin (see column 12, lines 36-39). Rink's claims 83 and 84 are drawn to methods for suppressing food intake and for control of appetite in a mammal (inclusive of humans) comprising administering a therapeutically effective amount of an amylin agonist such as ^{25,28,29}pro-h-amylin (see column 12, lines 27-34). Amylin agonist is administered in an amount of about 0.1 μg/kg/day (see column 95, lines 1-8) and 1-3 times a day (see column 21, lines 26 and 27). The amylin agonist can be s-calcitonin or h-amylin (see column 8, lines 35-38). Further, Rink *et al.* ('106) illustrate that administration of amylin alone did suppress food intake (see Figure 1). Rink *et al.* also discuss the art-recognized fact that amylin reduces food intake significantly in mammals (see the paragraph bridging columns 6 and 7). It is also taught, in both clinical and epidemiological studies, that obesity and type 2 diabetes mellitus are associated, and both may have common pathogenetic mechanisms. It is disclosed that weight reduction is often recommended as the first course of action for patients suffering from type II diabetes mellitus (see column 1, second paragraph).

Claims 1-3 are anticipated over Rink *et al.* ('106).

Rejection(s) under 35 U.S.C § 103

10) The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person. having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

11) Claims 1-10 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Rink *et al.*

(US 5,739,106) [Rink *et al.* ('106)] in view of Gaeta *et al.* (US 5,686,411).

The references of Rink *et al.* ('106) and Gaeta *et al.* have been applied in this rejection because they qualify as prior art under subsection (e) of 35 U.S.C. § 102 and accordingly are not disqualified under U.S.C. 103(a).

The teachings of Rink *et al.* ('106) have been explained above which do not disclose the specific doses, times and route of administration as recited in instant claims 4-10.

However, the safe administration to patients of specific doses of amylin agonist at the frequencies and by the routes of administration as recited in claims 4-10 is known in the art. For instance, Gaeta *et al.* teach that "[a]s will be recognized by those in the field, an effective amount of therapeutic agent will vary with many factors including the age and weight of the patient, the patient's physical condition ..... and other factors". Typical doses contain 0.1 to 1.0 mg of an amylin agonist compound and this range covers the one recited in claims 6-8. The composition may conveniently be provided in the form suitable for subcutaneous administration (see column 7, lines 37-40). It is further taught that a "suitable administration format may best be determined by a medical practitioner for each patient individually" (see column 7, lines 45-47), and that suitable "doses are readily determined by those in the art" (see column 8, lines 62 and 63). Further, the specific time period of administration is generally dose dependent and the time is determined based on standard treatment regimens. Generally, the dosage and periods of administration would vary with the age, sex, clinical condition, extent of the disease in the patient and can be further determined by one skilled in the art. The dosage and time period can also be determined or adjusted by a physician on an individual basis. The different times and routes of administration can be determined by routine experimentation and thus would have been obvious to one skilled in the art.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use Rink's method of controlling body weight, reducing food intake and suppressing appetite in mammals, including humans, by administering Rink's amylin agonist at doses, time periods and the route as taught by Gaeta *et al.*, since these can be readily determined based on the weight, age and physical condition of the patient as taught by Gaeta *et al.* or by routine experimentation and since Gaeta *et al.* have already shown that such doses, frequencies and the

route of administration are safe in mammals including humans.

Claims 1-10 are *prima facie* obvious over the prior art of record.

12) Claims 1-10 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Kolterman *et al.* (*Diabetologia* 39: 492-499, April, 1996) (Kolterman *et al.*, 1996), or Kolterman *et al.* (WO 96/40220) ('220), or Moyses *et al.* (*Diabetic Med.* 13 (suppl. 5): S34-S38, September, 1996), or Thompson *et al.* (*Diabetes* 46: 632-636, April 1997) in view of Cooper *et al.* (*Biochim. Biophys. Acta* 1014(3): 247-258, 1989, abstract) (Cooper *et al.*, 1989) and Rink *et al.* (US 5,739,106) [Rink *et al.* ('106)].

The reference of Rink *et al.* ('106) has been applied in this rejection because it qualifies as prior art under subsection (e) of 35 U.S.C. § 102 and accordingly is not disqualified under U.S.C. 103(a).

Kolterman *et al.* (1996) teach a method of treatment of patients with diabetes mellitus by subcutaneous administration of 30, 100 or 300 μg of pramlintide or AC137 (i.e., ^{25,28,29}pro-h-amylin) three times a day (abstract and page 493).

Kolterman *et al.* ('220) teach methods of treating type II diabetes mellitus comprising administering a therapeutically effective amount of an amylin agonist such as ^{25,28,29}pro-h-amylin, s-calcitonin and h-amylin (abstract and claims). ^{25,28,29}pro-h-amylin has been found to possess more desirable solubility and stability characteristics compared to human amylin (see page 13). It is taught that a suitable administration format may best be determined by a medical practitioner for each patient individually (see page 19). "The exact dose to be administered is determined by the attending clinician and is dependent upon where the particular compound lies within the above quoted range as well as upon the age, weight and condition of the individual". Administration may be preferably by subcutaneous injection. Amylin agonists such as ^{25,28,29}pro-h-amylin may be administered in single or multiple doses, for example, two (BID), three (TID), and/or four (QID) times per day. BID doses range from about 30 μg to 150 μg BID, more preferably from about 50 μg to 60 μg BID. TID doses range from about 30 μg to 150 μg, more preferably about 60 μg TID. QID doses range from about 30 μg to 60 μg QID, more preferably about 30 μg QID. These doses have been demonstrated to be effective in various human clinical trials and are

administered subcutaneously (see page 21).

Moyses *et al.* teach a method of treatment of human diabetic patients comprising administering pramlintide ($^{25, 28, 29}$pro-h-amylin) by subcutaneous injections in doses of 30 μg, 100 μg or 300 μg t.i.d. (see pages 36 and 38).

Thompson *et al.* teach a method of treating human subjects with diabetes, a clinical condition often associated with obesity, by administering subcutaneously 10, 30 or 100 micrograms (which falls in the dose range recited in claim 6) q.i.d. of Pramlintide, an amylin agonist analogue which "incorporates proline substitutions at positions 25, 28 and 29 of the amylin molecule" (see page 632).

Kolterman *et al.* (1996) or Kolterman *et al.* ('220) or Moyses *et al.* or Thompson *et al.* do not teach a method of treating or preventing obesity by administering pramlintide to a human subject.

However, Rink *et al.* ('106) teach the therapeutic effectiveness of $^{25, 28, 29}$pro-h-amylin, an amylin agonist, in controlling body weight, reducing food intake and suppressing appetite in mammals including humans (see abstract, and column 11, lines 25 and 26). Rink *et al.* ('106) teach that in both clinical and epidemiological studies, obesity and type 2 diabetes mellitus are associated, and both may have common pathogenetic mechanisms. Rink *et al.* ('106) disclose that weight reduction is often recommended as the first course of action for patients suffering from type II diabetes mellitus (see column 1, second paragraph).

Cooper *et al.* (1989) teach that "obesity which frequently accompanies" type 2 or non-insulin dependent diabetes mellitus (NIDDM) is a result of, rather than a risk factor for, NIDDM (see abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use Kolterman's method (1996 and '220) or Moyses' or Thompson's method of treating type 2 diabetes, which is frequently associated with overweight, with $^{25, 28, 29}$pro-h-amylin to treat obesity because, Rink *et al.* ('106) teach that $^{25, 28, 29}$pro-h-amylin is also effective in controlling body weight, reducing food intake and suppressing appetite in humans, and that there is an art-recognized clinical need for weight reduction in patients suffering from type II

diabetes mellitus. Since Cooper *et al.* (1989) teach that obesity is a result of NIDDM or type II diabetes, one of ordinary skill in the art would be motivated to produce the instant invention for the expected benefit of preventing NIDDM from advancing to or resulting in obesity. One of ordinary skill in the art would have had a reasonable expectation of success in using Kolterman's (1996 and '220) or Moyses' or Thompson's method of treating diabetes also for the treatment of obesity, because these two associated clinical conditions are believed to share the common pathogenetic mechanisms as taught by Rink *et al.* ('106). Given the close association between diabetes and obesity, the shared pathogenetic mechanisms, the art-recognized recommendation that weight reduction be the first course of action for patients suffering from type II diabetes mellitus as taught by Rink *et al.* ('106) and given the Rink's disclosure of the therapeutic effectiveness of an amylin agonist, such as, ^{25,28,29}pro-h-amylin, in controlling body weight, reducing food intake and suppressing appetite in mammals including humans, one skilled in the art would have been motivated to extend Kolterman's (1996 and '220) or Moyses' or Thompson's method of treating diabetes using an amylin agonist, such as, ^{25,28,29}pro-h-amylin, to the treatment of obesity, with a reasonable expectation of success.

Claims 1-10, as a whole, are *prima facie* obvious over the prior art of record.

13) Claims 11-15 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Kolterman *et al.* (*Diabetes Care* 18: 1179-1182, August 1995) (Kolterman *et al.*, 1995) in view of Rosenbloom *et al.* (*Am. J. Dis. Child.* 131: 881-885, 1977), Rink *et al.* (WO 92/20367) (Rink *et al.*, '367) and Morley *et al.* (*Am. J. Physiol.* 267: R178-R184, 1994) (Morley *et al.*, 1994).

Kolterman *et al.* (1995) teach the administration of ^{25,28,29}pro-h-amylin and of amylin agonist therapy in patients with type 1 diabetes mellitus (see page 1181, column 3). Kolterman *et al.* are silent about the status of insulin-induced weight gain in the type 1 diabetic patients that they treated and the effect of amylin or an amylin agonist on weight gain.

However, Rosenbloom *et al.* teach that insulin overdosage in type 1 diabetic patients leads to excessive appetite and weight gain (see abstract).

Rink *et al.* ('367) disclose that amylin can act as an appetite suppressant (see page 11).

Morley *et al.* (1994) teach a method of reducing food intake in obese and diabetic subjects by administering upto 200 micrograms of amylin per kg (see abstract and page R179).

Given the art-recognized association between insulin overdosage in IDDM and excessive appetite and weight gain as taught by Rosenbloom *et al.*, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use Kolterman's (1995) method of treatment with $^{25, 28, 29}$pro-h-amylin for type 1 diabetic patients suffering from insulin-induced weight gain, to produce the instant invention, because amylin is known in the art to act as an appetite suppressant as taught by Rink *et al.* ('367). A skilled artisan would have had a reasonable expectation of success in using Kolterman's (1995) method in reducing insulin-induced weight gain in type 1 diabetic patients, since amylin is known to reduce food intake in obese and diabetic subjects as taught by Morley *et al.* (1994).

Claims 11-15, as a whole, are *prima facie* obvious over the prior art of record.

Relevant Prior Art

14) The prior art made of record and not relied upon in any of the rejections is considered pertinent to Applicants' disclosure:

- Meglasson (US 5,900,435) discloses the art recognized need for therapy to treat or prevent obesity (see column 4, lines 32-33). Meglasson teaches that "obesity is considered to be of importance in the development of NIDDM" and that "weight reduction is considered to be the primary medical therapy for NIDDM patients" (see column 9, first paragraph).
- Weisser *et al.* (*J. Clin. Pharmacol.* 37(6): 453-473, 19 June 1997) teach the association between amylin and obesity and the possible role of amylin in weight reduction (see page 467).
- Morley *et al.* (*Am. J. Physiol.* 267: R178-R184, 1994) teach the role of amylin as a peripherally acting satiety agent (abstract).
- Morley *et al.* (*Can. J. Physiol. Pharmacol.* 73: 1042-1046, 1995) teach that amylin decreases food intake in mice and rats when delivered both peripherally and directly into the CNS (see abstract).
- Lutz *et al.* (*Physiol. & Behavior* 55(5): 891-895, 1994) teach that low doses of amylin reduces food intake in rats by i.p. injection (see abstract).
- Kolterman (*Diabetic Med.* 14(suppl. 1): s35-s38, 13 June 1997) teaches a method of treatment of diabetes mellitus comprising subcutaneous injections of 10, 30 and 100 μg of

pramlintide (see page s36).

- An article published in *Exp. Opin. Ther. Patents* 4(11): 1383-1384, 1994 discloses amylin and related peptide analogues for a "myriad of therapeutic applications" including treatment of obesity (see pages 1383 and 1384).

- Koopman *et al.* (*Neth. J. Med.* 41(1-2): 82-90, 1992) suggest the involvement of amylin in the pathophysiology of obesity, type II diabetes and insulin resistance (see abstract).

- Ludwik (*Wien Klin. Wochenster* 109(11): 379-383, June 6, 1997, abstract) teaches the subcutaneous administration of the amylin agonist, pramlintide, in diabetics and the association between obesity and circulating amylin (see abstract).

- Rowland *et al.* (*CNS Drugs* June 7 (6): 419-426, 1997) teach the role of amylin in the treatment of overeating and obesity (see abstract and page 422).

- Porte (*Diabetes* 40(2): 166-180, 1991) teaches obesity, its associated insulin resistance and the role of amylin (see abstract).

- Young *et al.* (*Drug Dev. Res.* 37: 231-248, 1996) teach that the "search for a pharmaceutically superior compound with the biological actions of human amylin resulted in the identification of [Pro $^{25, 28, 29}$] human amylin, assigned the U.S.-adopted name (USAN), pramlintide" (see page 231). Actions occurring with varying doses of amylin include reduction of appetite (see page 232).

- Cooper (US 5,124,314) teaches a human amylin composition for treatment of diabetes mellitus (claim 9 and abstract) including type 2 diabetes (see column 3, lines 63-66). Amylin is given by parenteral subcutaneous administration (last sentence bridging columns 5 and 6).

- Cooper *et al.* (US 5,280,014) teach a method of treatment of obesity on a subject comprising administering to a mammal an effective amount of an amylin antagonist (claims). One such compound, CGRP8-37, which acts as a partial antagonist is also an amylin agonist (see column 11, lines 3-6).

- Janes *et al.* [*Diabetes* 45 (suppl. 2): A865, 1996, p. 235A] teach that amylin is deficient in type I diabetes and some cases of type II diabetes, and that human amylin has a propensity to aggregate and has poor solubility. It is further taught that "different combinations

of substitution within the human amylin sequence at positions 25, 28 and 29 with proline residues and at position 18 with an arginine residue were identified which greatly reduced the aggregation and precipitation of human amylin". Pramlintide, also designated [Pro $^{25, 28, 29}$] human amylin or AC137 exhibits the best overall properties. "By substituting three residues of the human amylin sequence with proline, a novel compound was discovered that retains the desired biological activity of human amylin whilst possessing superior physicochemical and other characteristics" (see abstract).

- Gaeta *et al.* (US 5,686,411) teach a method of treatment of diabetes mellitus in a mammal (inclusive of humans) comprising administering a therapeutically effective amount of an agonist analogue of amylin (see claim 34) such as $^{25, 28, 29}$pro-h-amylin (see claim 35).

- Colburn *et al.* (*J. Clin. Pharmacol.* 36: 13-24, 1996) teach the administration of 30-300 μg of AC137 or $^{25, 28, 29}$pro-h-amylin tripro-human amylin to human subjects with insulin-dependent diabetes mellitus (see abstract and page 14).

- Thompson *et al.* (*Abstract Book*, 55th *Annual Meeting and Scientific Sessions*, June 10-13, 1995, Georgia World Congress Center, Atlanta, Georgia. *Diabetes* 44: suppl. 1, May 1995, Ab. 469, p. 127A) teach a method of treating type II diabetic patients comprising subcutaneous injections of AC137 (see abstract).

- Morley *et al.* (*Peptides* 12: 865-869, 1991) teach that amylin decreases food intake in both diabetic and non-diabetic mice following intracerebroventricular administration (abstract). Amylin may have both central and peripheral sites of action. Unlike amylin, CGRP, an amylin agonist, only inhibited feeding after central and not after peripheral administration. Amylin is considerably more potent than CGRP at suppressing food intake. Morley *et al.* suggest the possible role of amylin in the pathophysiology of obesity seen in some individuals with type II diabetes mellitus (see page 868).

Remarks

15) Claims 1-15 stand rejected.

16) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1.

The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242, which is able to receive transmissions 24 hours a day and 7 days a week.

17) Any inquiry concerning this communication or earlier communication(s) from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. The Examiner can normally be reached on Monday to Friday from 8.00 a.m to 4.00 p.m. A message may be left on the Examiner's voice mail service.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SD
S. Devi
Patent Examiner
July 2000